Section of Pathology

President Professor Ronald Hare MD

Meeting October 15 1963

President's Address

The Transmission of Respiratory Infections

by Professor Ronald Hare MD
(*Department of Bacteriology, St Thomas's Hospital Medical School, London*)

When infection of the respiratory tract occurs, it can be assumed that the organisms will generally have reached the recipient at the start of the incubation period of the disease, and have come from the nose or throat of another human being who is actively infected or is a carrier. The mechanism by which this transfer is brought about must be highly efficient because some at least of these diseases are extremely infectious. But although there are theories in plenty purporting to explain how they are transmitted, fiction rather than fact plays all too large a part in their formulation. It may, therefore, prove useful if I discuss the matter in some detail.

I think we can assume that, however it is effected, transmission will almost always involve three distinct and largely independent steps: The first is the egress of the organisms into the outside world; the second involves their survival and transportation to the nasal orifices or lips of another person; and the third is their passage from these portals of entry to their site of multiplication in the nose, throat or lungs.

I shall say very little about the third of these steps. For many years it was firmly believed that it followed contact between a contaminated object and the nose or lips of the recipient. But although this can occur, it is more probable that the organisms are transported on airborne particles of some kind.

As will be shown, most of them are more than 4 μ in diameter and therefore large enough to be trapped by the highly efficient filtering mechanism constituted by the saliva in the mouth and the mucous blanket on the membranes of the nose and pharynx (Harper & Morton 1953, Druett *et al.* 1953). Those that are sufficiently small to escape can penetrate as far as the terminal bronchioles and the alveoli, and it is on such particles that pulmonary organisms such as tubercle bacilli and some of the viruses are probably carried (Hatch & Hemeon 1948, Wells *et al.* 1948, Druett *et al.* 1953). In this way, most respiratory organisms reach the very areas that are their natural habitats.

The first two steps, egress of the organisms from the donor and their conveyance to the recipient, are much more controversial and are the main theme of this Address.

In regard to the egress of the organisms, it is extremely improbable that even the smallest of them can leave the respiratory tract by carriage in the water vapour that evaporates from the mucous membranes to saturate the expired air (Hare 1940, Hirshfeld & Laube 1941, Bourdillon *et al.* 1942). Something much more active than this is required to dislodge them and get them out of the respiratory tract. This can take four forms: swallowing, expectoration in sputum and saliva, expulsion in droplets or outflow in saliva or nasal mucus.

Swallowing

This is probably the most efficient method. Nearly all the organisms, no matter where they multiply, will, in one way or another, reach the pharynx and be swallowed in the saliva. But few are likely to survive and emerge in the fæces. Even if they do, it is so improbable that they will play any part in the dissemination of respiratory diseases that this method need not be discussed further.

Expectoration

Expectoration in sputum or saliva is also efficient, but neither vehicle is likely to impinge directly on the mouth or nose of another person. Their organisms can, however, reach him on airborne particles disseminated from the masses after drying. But since uninhibited spitting and expectoration are both unusual and sputum is produced in only comparatively few infections, this method of transmission, although of undoubted importance in tuberculosis (Cornet 1889, 1904; Chaussé 1914*c*, 1916), can play only a small part in the spread of most respiratory infections.

Expulsion

Flugge (1899) was the first to show that micro-organisms can be expelled in droplets from the respiratory tract and in this way reach another person. Their study is not easy because practically all of them are invisible and until recently indirect methods had to be used to obtain information about them. This generally involved the instillation of a harmless indicator organism, such as *Chromobacterium prodigiosum*, into the mouth, catching the expelled droplets on culture plates, counting the numbers of colonies after incubation and assuming that the number obtained bore close relationship to the number of droplets expelled. By this method Flugge, and more particularly his pupils and successors, Lastschenko (1899), Doust & Lyon (1918) and Winslow & Robinson (1910), ascertained that very few if any droplets are produced during quiet breathing but that they are expelled during activities such as talking, coughing, blowing and sneezing.

Since very large numbers of the indicator organisms may sometimes be expelled, the assumption has over and over again been made that pathogenic organisms will be emitted in equal or even larger numbers when the subject is infected or is a carrier. But anyone who has tried to prove this has generally been forced to admit that in fact the expulsion of pathogens is a comparatively uncommon event. In view of this wide divergence of fact from theory, I will have to discuss the whole process of droplet production in some detail.

Production of droplets: There seems to be no doubt that droplets are produced as a result of atomization of the secretions (Flugge 1897, Jennison 1941). That is to say, the expired air passing over the surface of the mucous membrane drags some of the secretion off in the form of a long tongue which undergoes fragmentation to form spherical droplets whose diameter may range from 1 μ to 2 mm. For this, the velocity of the air must be more than about 4 metres per second (Flugge 1897). This is never reached when breathing quietly but if the lumen of the respiratory tract is narrowed and the local velocity of the airstream raised by forcing air through the constriction, atomization of the secretions at this point can occur.

Anatomical peculiarities may narrow the air passages sufficiently for this purpose. A tumour or an œdematous mucous membrane may, for example, partially block the nasal cavity and so bring about expulsion of droplets from the nose if air is deliberately forced past the obstruction. Adults seldom attempt this but children do when they get a cold. This may explain the presence of *Staphylococcus aureus* in the atmosphere near 'cloud babies' (Eichenwald *et al.* 1959). Thick viscid sputum in the bronchi in whooping-cough and other pulmonary infections may also lead to the expulsion of droplets.

Under most circumstances the necessary constriction is caused by muscular action. This can occur at only a few sites. It is most efficiently produced at the front of the mouth where atomization of the saliva is brought about by apposition of the lips, tongue and front teeth in such activities as blowing, whistling, talking, coughing and sneezing. This results in the production of about one million droplets as a result of one sneeze, 5,000 during one cough and 250 when talking for one minute (Duguid 1946*b*).

Any organisms present in the saliva will be expelled in some of these droplets and will form colonies if a culture plate is held in the droplet stream. The numbers expelled depend very largely on the amount of force employed so that a fully grown man with a deep bass voice usually expels a great many more than does a slightly built female.

The nasal cavity, on the other hand, is quite unsuited for the production of droplets. It is, over the whole of its length, a rigid tube that cannot be constricted by any form of muscular action, except in one place, the vestibule. Even so, the only activity that brings it about is the highly abnormal one known as snorting, that is to say, forcing air through the nose while contracting the alæ nasi muscles. But neither these, nor any of the other nasal muscles, constrict the vestibule during common activities such as speaking, or coughing. Even sneezing does not involve contraction of these muscles, except possibly when an attempt is made to stifle it. There is, therefore, no reason why droplets should be expelled from the nose except under somewhat unusual circumstances.

Assuming that the number of commensals reaching culture plates held beneath the nose gives an indication of the number of droplets expelled, study of 10 normal persons showed that an average of 7·8 colonies grew on plates exposed during 5 minutes' mouth-breathing, 6·4 when nose-breathing, 13·4 when talking and 3·4 as a result of 6 coughs. Such results might have been expected, but few would have suspected that only 4·1 colonies would be found on the plates exposed during one sneeze. When, on the other hand, the alæ nasi were purposely contracted during 12 snorts, no less than 415·4 organisms reached the plates (Hare & Thomas 1956). Very similar results were obtained with another series of individuals who had colds with increased secretion. But when droplets expelled from the mouth were studied, entirely different results were obtained, an average of 203·5 bacteria-contaminated droplets being expelled in 5 minutes' talking, 50·2 as a result of 6 coughs and no less than 2,000 by one sneeze. On the whole, therefore, the nose, as a droplet-producing organ, leaves a great deal to be desired.

With the exception of the front of the mouth, every other part of the respiratory tract is equally deficient and for much the same reasons. Nevertheless, a few droplets are produced from the pillars of the fauces or the vocal cords in the acts of hawking or dry coughing, and as already mentioned, violent paroxysmal coughing to dislodge mucus may bring about expulsion of a few droplets from the bronchi (Ziesché 1907). But none of these sites will bear comparison, as droplet-producing areas, with the front of the mouth.

Presence of pathogens in the droplets: From the above discussion, it should be obvious that in so far as the transmission of respiratory infections by droplets is concerned, the front of the mouth is the key area because most of the droplets come from there. This renders the flora of the saliva in the front of the mouth a matter of great importance, because it is improbable that pathogens will be expelled unless they are present in the saliva in this position.

The most efficient way to ensure this would be for the organisms to multiply in the front of the mouth. Some can probably do so. Such organisms include those responsible for Vincent's angina and thrush and the viruses of smallpox, chickenpox and measles, all of which produce lesions on the buccal mucous membranes as well as on the hard and soft palates, the fauces and the pharynx. To these must be added the virus of mumps because it is known to reach the mouth in saliva. Nevertheless, it is very necessary to add that there is no experimental proof that any of these organisms are in fact expelled in droplets.

It is highly improbable that any other respiratory pathogens actually multiply anywhere in the mouth itself except under somewhat unusual circumstances. Is it possible, therefore, for one or other of them to be conveyed to the front of the mouth and in this way to become capable of expulsion in droplets?

Apart from the work of Bloomfield (1921), dealing for the most part with commensals in uninfected subjects, very little is known about the transfer of organisms from one part of the human respiratory tract to another. But for several reasons, they may have more difficulty in reaching the all-important anterior part of the mouth than is usually realized. The comparative isolation of the mouth itself from the pharynx and the rest of the respiratory tract is in itself an impediment. But even if organisms from the pharynx pass through the pillars of the fauces, they will immediately encounter the backward flow of the saliva (Bloomfield 1922*a*, *b*) which, together with deglutition, may drive them back again. Even if they do reach the front of the mouth they may not survive very long because they may encounter antibacterial substances such as that described by Gordon (1916) and a micro-environment quite unlike that of their normal habitat.

That all this is not mere theory can, to some extent at least, be proved by experiment. When, for example, an organism such as *Streptococcus pyogenes* is multiplying as close to the mouth as on the tonsils, in scarlet fever or tonsillitis, it is not always possible to isolate it from the saliva in the front of the mouth (Bloomfield & Felty 1924). Hamburger (1944) found it in 68% and Duguid (1946*a*) in only 13% of such patients. Similarly, Hare (1940) failed to isolate it from the saliva of 2 out of 9 and Rubbo & Benjamin (1953) from one out of 6 symptomless carriers. *Corynebacterium diphtheriæ* may apparently behave in the same way; Duguid (1946*a*) isolated it from the saliva of only 10 of 50 patients with diphtheria.

If then organisms, even when present in large numbers on the tonsils of patients or carriers, fail to traverse the short distance to the front of the mouth, it is perhaps not surprising that Bloomfield & Felty (1924), Colebrook (1933), Paine (1935) and Hare (1940) all observed that streptococci are only infrequently expelled when talking, coughing or sneezing. Duguid (1946*a*), too, found that when 87 patients with scarlet fever coughed six times at culture plates, *Strep. pyogenes* was expelled by only 39 (44·8%) and *C. diphtheriæ* by only 10 (20%) of 50 patients with diphtheria. Even when they were expelled, much fewer than 10 colonies generally appeared on the plates; on most, only one or two.

Since so few tonsillar organisms get to the main droplet-producing area in the front of the mouth, there is no reason to suppose that those multiplying in more distant parts of the respiratory tract will fare any better. Those in the pharynx, for example, are much more likely to be swallowed than driven into the mouth, if only because this takes conscious effort on the part of the individual; and certainly Bloomfield & Felty (1924) found that *Escherichia coli* placed on the pharyngeal wall was not expelled when talking, coughing or sneezing.

Organisms that multiply on the mucous membranes over the turbinates have still further to travel if they are to reach the front of the mouth so that it is equally improbable that they will be expelled in buccal droplets. Nor are they likely to be expelled by way of the nose, largely because nasal droplets are only expelled in any number when snorting, not when talking, coughing or even sneezing. And certainly *Staph. aureus*, which multiplies much further forward in the vestibule, is only expelled by carriers on rare occasions (Hare & Thomas 1956, Shooter *et al.* 1959). In view of all this, it is extremely improbable that other and possibly more important nasal organisms such as *Neisseria meningitidis* and the viruses of colds and influenza will be expelled in droplets from either the nose or mouth: an almost revolutionary conclusion in view of the fact that all three diseases are universally thought to be transmitted by droplets.

There remain for consideration organisms that multiply in the lungs. Some may, as is apparently possible in whooping-cough and tuberculosis, reach the outside world in droplets produced as a result of coughing when there is some form of obstruction in the bronchi. But contamination of the saliva by sputum is more likely to secure their egress in droplets. This can certainly occur in tuberculosis: *Mycobacterium tuberculosis*, which has been found in the saliva of about half the patients with pulmonary tuberculosis examined by Chaussé (1914*a*), Gloyne (1922) and Duguid (1946*a*), can be picked up on glass slides held in front of the mouth while coughing. But only about half the patients expel them and the numbers expelled are low.

Thus, so far as the transport of pathogens by droplets is concerned, only those coming from the mouth need be seriously considered. These are most likely to contain pathogens if they multiply in the mouth or can reach it in sputum. Tonsillar and pharyngeal organisms are much less likely to do so and nasal organisms virtually never.

Behaviour of droplets after expulsion: This depends largely on their size at the time they leave the mouth (Lange & Keschischian 1925). Those smaller than about 0·1 mm (100 μ) in diameter become droplet nuclei (Wells 1934, Duguid 1945). Those larger than this remain droplets and are sometimes referred to as Flugge droplets.

Behaviour of the larger (Flugge) droplets: Comparatively few of the droplets are large enough to come within this category by remaining droplets after leaving the mouth. Indeed, of the 1,000,000 or so expelled when sneezing, only 9,700 will do so; when coughing, only 198 of the 5,000; and when talking, 14 of the 250 droplets produced.

Such droplets consist of spherical or nearly spherical masses of the secretions (for the most part saliva) from which they have come. Their sizes vary considerably, the smallest being about 0·1 mm (100 μ) in diameter and the largest 1 or even 2·0 mm. They are expelled with a fair amount of force and, being relatively large, carry a good deal of momentum. These factors, together with others such as the resistance imposed by the atmosphere and the effect that gravity may have on them, will determine how they behave after leaving the mouth.

The initial velocity of the droplets naturally depends on the activity producing them, so that although it is only about 16 metres per second when talking (Strauss 1922) it can be as much as 150 when sneezing (Jennison 1941). When the head is facing downwards, these differences are of little importance because gravity acts in the same direction as their initial motion and all the droplets fall almost vertically, impinging on whatever is below. But when the head is upright, gravity acts perpendicularly to their line of motion. This alters their behaviour radically. Study of photographs (Weyrauch & Rzymkowski 1938, Jennison 1941) or experiments in which normal subjects, with indicator organisms in the mouth, talk, cough or sneeze in front of a quarter circle of culture plates disposed in front of and below the mouth in the sagittal plane of the head (Hare 1940, Hare & Mackenzie 1946), would suggest that during talking their initial velocity is so low that the resistance of the atmosphere brings them to a halt very soon after they have left the mouth. They then begin to fall vertically. In coughing, blowing and even more so in sneezing, there is more force behind them so that the horizontal portion of their trajectory can be much longer; but even so they eventually fall to the ground.

There is accordingly considerable variation in the distance likely to be travelled in a horizontal direction. In sneezing, some can be propelled as much as 4–5 feet (Flugge 1899, Bourdillon &

Lidwell 1941) but in talking little more than a few inches (Hare 1940). A further limitation of their sphere of activity comes from their inability to spread sideways very far from the sagittal plane of the head.

Thus, so restricted is their field of fire that unless the nose or mouth of the recipient is below and directly in line with that of the donor, very few of the droplets produced as a result of any form of activity are likely to reach him. Nevertheless, their organisms may still get to him by an indirect route involving their inhalation on particles released into the atmosphere from droplets which have dried following their deposition. But even when this alternative is taken into consideration, it would seem that, on the whole, the one reasonably certain method of transmitting infection by droplets would be by declaiming the hot words of love directly into the respiratory passages of the beloved.

How long pathogenic organisms in droplets can survive after leaving the mouth is still largely unknown. It would, however, appear from the work of Hemmes *et al.* (1960) and Harper (1961) that the relative humidity of the atmosphere plays an important part. Using droplets produced by artificial means they found that influenza, vaccinia and encephalitis viruses were killed when the relative humidity is high, as obtains in summer, whereas that of poliomyelitis survived. It, in its turn, was killed at low relative humidities.

What influences other factors such as light and other radiations may have on organisms in droplets is still quite unknown.

Behaviour of the smaller droplets (droplet nuclei): A very high proportion of the droplets expelled are smaller than 0·1 mm (100 μ) in diameter, and therefore come into this category. A series of measurements carried out by Duguid (1945) showed that of the 1,000,000 droplets of all sizes produced as a result of one sneeze, about 990,500 come within this size range. In coughing 4,775 of the 5,000, and in talking 236 of the 250, droplets produced are similarly less than 0·1 mm in diameter. The great majority of them are very much smaller than this. Of the 990,500 produced as a result of one sneeze, for example, no less than 851,658 are only 1–4 μ in diameter.

Such droplets behave quite differently from the larger Flugge droplets. This is due to the fact that under ordinary conditions of temperature and humidity virtually all the water contained in them disappears by evaporation almost as soon as they emerge from the mouth leaving only the non-volatile residues such as salts, tissue debris and micro-organisms originally present in them. As a result they shrink to between one-fifth and one-third of their original diameter (Wells 1934, Wells & Stone 1934, Duguid 1946*b*). Wells called such residues droplet nuclei.

Being so small, whatever momentum they possessed on leaving the mouth disappears almost at once. They cannot, therefore, overcome the resistance of the atmosphere so that they neither travel forwards nor fall under the influence of gravity. Suspended in the air in this way, the larger slowly sink and may have reached the ground within a few minutes, whereas the smallest may remain airborne for twenty-four hours or more (Phelps & Buchbinder 1941, Duguid 1946*b*). Thus, for a time, they are at the mercy of air currents and can be carried long distances (Wells & Wells 1936, Trillat 1938). This gives them many advantages over the heavier and therefore less mobile Flugge droplets which have been persistently stressed in the many papers published by Wells. Nevertheless, there are many reasons for thinking that droplet nuclei are very much less efficient transporting agencies than is usually supposed.

In the first place, there is evidence that, unless large numbers of indicator organisms have been placed in the mouth, only about 7–8% of the enormous numbers of droplet nuclei that are produced will contain organisms of any kind (Duguid 1946*b*).

Secondly, the very small, slow-settling, highly mobile droplet nuclei prominent in photographs of sneezes, for example, are not in fact those that carry organisms. They are carried by the largest, heaviest and therefore least mobile of those produced. Thus, the diameters of 62% of those that carry bacteria have been shown to lie between 4 and 18 μ, only 22% being smaller than this (Lidwell *et al.* 1959). Duguid (1946*b*) obtained somewhat similar results and also showed that the great majority of droplet nuclei that are as large as this will probably fall to the ground within a minute of expulsion, very few being likely to remain suspended for as long as ten minutes.

Thirdly, for reasons already discussed, pathogens will not be present in any number in droplet nuclei unless they can reach the droplet-producing area in the front of the mouth. It is, therefore, to be presumed that organisms that actually grow in the mouth, such as the viruses of smallpox, chickenpox and measles, can be expelled in droplet nuclei but even so, this has not yet been actually proved.

Organisms that multiply in the nose on the other hand, such as the viruses of colds and influenza, cannot very well be expelled at all except possibly under somewhat unusual circumstances such as snorting.

Those that multiply in the lungs and pharynx and on the tonsils stand a slightly better chance, but even if they do reach the front of the mouth they are more likely to be expelled in droplets than in droplet nuclei because calculations using determinations by Duguid (1946*b*) of sizes of droplets and droplet nuclei produced, show that in sneezing only 14·5%, in coughing 10·7% and in talking 10·8% of the saliva that is atomized goes into droplet nuclei. Thus, only 10–15% of each species of organism including pathogens present in the saliva in the front of the mouth will be expelled in droplets small enough to become droplet nuclei.

When, therefore, any particular species is present in only small numbers, as is frequently the case with tonsillar and pulmonary organisms such as *Strep. pyogenes* (Hamburger 1944), *C. diphtheriæ* and *Myco. tuberculosis* (Duguid 1946*b*), there is a possibility that they may not be detectable in the droplet nuclei. Indeed, my own work (Hare 1940) suggested that it would require steady talking for 60 minutes or 113 coughs by a carrier to produce only one droplet nucleus containing *Strep. pyogenes*. And certainly I was unable to isolate this organism in seven attempts with four carriers who talked for 5 minutes while from 6·55 to 7·55 cubic feet of air taken from a point only 12 inches away was sampled in a Wells air centrifuge.

It would seem probable that others have been equally unsuccessful because no one, so far as I am aware, has yet shown that, under properly controlled conditions, the droplet nuclei emitted by a patient infected by, or a carrier of, a respiratory pathogen do, in fact, contain the pathogen in question. On the whole, therefore, despite the contentions of Wells, it is extremely doubtful whether droplet nuclei play any important part in the transmission of respiratory infection.

Outflow

This is the fourth and so far as we know, the only remaining method by which organisms can leave the nasopharynx. It is largely but not entirely a consequence of our inability, asleep or awake, to keep our fingers and handkerchiefs away from our noses and mouths so that any organisms in our saliva or nasal secretion quickly reach our skin, clothing, bedding and environment generally. Although this possibility must have been recognized for many years, it was not until 1910 that it was considered seriously when Chapin (1910) in his 'Sources and Modes of Infection' described it as follows: 'Everyone is busily engaged in this distribution of saliva, so that the end of each day finds this secretion freely distributed on doors, window sills, furniture and playthings in the home, the straps of trolley cars, the racks and counters and desks of shops and public buildings and indeed upon everything that the hands of men touch.'

Nasal secretion, particularly when there is infection, can reach the environment even more easily than can saliva. It is this dissemination of nasal and buccal secretion that, for want of a better term, I have called outflow.

Chapin did not actually prove that the organisms accompany these secretions and indeed, it was not until 1939 that this was forthcoming when it was shown that *Staph. aureus* from the nose of a carrier could be isolated from the skin of the hands and other parts of his body (Gillespie *et al.* 1939). Subsequent work by Williams (1946), Hare & Thomas (1956) and Hare & Ridley (1958) showed that this had undoubtedly occurred as a result of outflow and that many areas of skin together with the handkerchief and the clothing might be contaminated by this organism and sometimes very heavily. During the same period Hare (1941) showed that when *Strep. pyogenes* is present in the nose, it too can be readily conveyed to the skin, clothing and bedding. Quite large numbers may be found: 100,000 for example, on an area six inches square on the lower sheet of a carrier's bed, being by no means unusual (Hamburger *et al.* 1945).

If these two organisms can reach the person and environment so easily in such large numbers, it is a justifiable conclusion that other nasal organisms such as the viruses of colds and influenza will similarly find egress in this way. But there is as yet no direct proof of this.

Nor is there proof that organisms that multiply in the mouth such as the viruses of smallpox, chickenpox and measles can similarly find egress by outflow in saliva. But indicator organisms have certainly been isolated from the clothing within an hour of their being placed in the mouth (Hare & Mackenzie 1946) and fluorescent substances in the mouth quickly become widely disseminated to many places on the person and in the environment. It is, therefore, probable that buccal organisms may similarly find egress in saliva.

This conclusion is, to some extent, confirmed by the finding that *Strep. pyogenes*, multiplying on the tonsils of carriers (and not in the nose), can undoubtedly obtain egress in saliva and as a result be found on the skin, clothing and bedding (Hare 1941). But as tonsillar organisms may fail to reach the saliva in the front of the mouth of a proportion of carriers or patients it is perhaps not surprising that streptococci are less likely to reach the person and environment than when they come from the nose, and fewer will be found there, in fact only about one-tenth as many (Hamburger *et al.* 1945).

Organisms that infect the lungs can only find egress by outflow if they reach the mouth in sputum and so contaminate the saliva. Expectorated sputum particles together with droplets of saliva produced while coughing probably add their quota. But whatever the reason, very heavy contamination by *Staph. aureus* of the whole contents of the bed and the floor in the neighbourhood has been found when patients have staphylococcal pneumonia (Hare & Cooke 1961). Those with pulmonary tuberculosis may also contaminate themselves and their surroundings, *Myco. tuberculosis* having been found on the bedding (Chaussé 1914*c*, Cornet 1889), clothing (Friberger 1909), handkerchief (Chaussé 1914*c*), the hands (Cumming 1920, Ostermann 1908) and the dust of wards (Cornet 1889, Rogers 1920). Lastly, *Diplococcus pneumoniæ* has been found in the dust of rooms in which there were cases (Stillman 1917).

There seems little doubt, therefore, that outflow can lead to widespread and sometimes heavy contamination of the person and environment by organisms coming from the nose, tonsils, lungs and presumably the mouth as well.

Factors involved in the outflow of micro-organisms: There is no reason to suppose that outflow occurs in any different manner from that described by Chapin except for the fact that nasal organisms are much more likely to find egress than those in the mouth.

There are, however, wide variations in the number of organisms likely to be found. While this may be, in part, due to variations in the number available in the respiratory tract, the site where they are multiplying, the personal habits of the subject and the amount of secretion available, it is probable that other as yet unknown factors also play a part.

Furthermore, survival may prove a serious problem because the organisms become subject to the lethal effects of physical agents such as desiccation and ultraviolet light as well as the natural bactericidal power of the skin itself as soon as they emerge. Nor is it at all certain that even when an organism remains alive, it remains capable of causing infection. The work of Rammelkamp and his colleagues (Rammelkamp *et al.* 1958) would certainly suggest that *Strep. pyogenes* may become progressively incapable of causing tonsillitis once it has left the throat of a patient.

Transmission to the recipient: Chapin believed that the organisms on the person and in the environment can only get to another individual by what he called contact infection; that is, by actual physical contact of the contaminated surfaces or some object they have touched, with the nose or mouth of the recipient. But in 1937 Brown & Allison found, when investigating the causation of relapses in scarlet fever, that another method of transport was available that had not been suspected by Chapin or, indeed, anyone else. This consists of particles contaminated by *Strep. pyogenes* that can be detected in the air of scarlet fever wards in large numbers and which are almost certainly responsible for the cross-infections causing the relapses. Brown & Allison did not determine how the streptococci reached the atmosphere but there was evidence to suggest that they had come from the bedding. They were certainly not carried by droplets or droplet nuclei. Nor could they be particles of dried sputum because such patients do not produce it.

Not long afterwards, it was clearly established by Thomas & Van den Ende (1941) that the airborne streptococci had come from the bedding and that their presence in the air depended to a large extent on some form of agitation to release them. A little later, Hamburger *et al.* (1944) and Green *et al.* (1945) found that *Strep. pyogenes* could similarly be dispersed into the atmosphere from the clothing of ambulant carriers as a result of such activities as walking, dancing, waving the arms about, dressing and undressing.

It had thus become evident in the 1940s that in addition to vehicles such as particles of sputum, droplets and droplet nuclei, another vehicle altogether could apparently convey at least one organism, *Strep. pyogenes*, from person to person. What is more, the particles containing this organism might, under certain circumstances, number as many as 150 to 200 per cubic foot of air, a number far larger than is ever likely to be obtained as a result of its expulsion in droplets or droplet nuclei. It is, therefore, not very surprising that inhalation of such particles is now generally recognized as the usual method by which *Strep. pyogenes* is acquired.

Somewhat similar investigations carried out a year or two later suggested that staphylococci are transmitted in the same way when it was found that aerial contamination by *Staph. aureus* might be found in the neighbourhood of carriers who were exercising or, in fact doing anything that might dislodge organisms that had reached the skin or clothing (Duguid & Wallace 1948, Hare & Thomas 1956, Hare & Ridley 1958).

A third organism that can similarly become airborne is *Myco. tuberculosis*. It can certainly reach the skin, bedding and clothing of patients with pulmonary tuberculosis and can be liberated into the atmosphere by brushing the clothes or shaking the bedclothes and handkerchief (Chaussé 1914*c*). It has also been detected in the air of wards at points as high as 80 cm above the patient (Chaussé 1914*b*). Riley *et al.* (1959), too, found it in the exhaust ducts of the ventilating system.

Lastly, there is high probability that other organisms, *Dip. pneumoniæ*, *C. diphtheriæ* and *N. meningitidis*, may similarly be conveyed on airborne particles because they have been found in the air or in the dust of wards in which there were cases, but virtually nothing is known as to how they got there (Stillman 1917, Wright *et al.* 1941, Eagleton 1919).

Factors involved in the dissemination of particles from the contaminated surfaces: The dispersal of particles containing the organisms can only occur if there is some form of activity such as friction or washing with soap and water when the organisms are on the skin (Hare & Thomas 1956) or shaking, brushing and similar forms of agitation when they are on the clothing (Duguid & Wallace 1948). Similarly, making the bed or merely drawing one layer of bedclothes over the remainder, will bring about dispersal of those on the bedding (Thomas & Van den Ende 1941, Rubbo *et al.* 1962).

The amount of violence also plays a part in determining the number of organisms dispersed. The number of *Staph. aureus* falling on to culture plates exposed in the neighbourhood of a heavily contaminated carrier, for example, can vary from none at all when he is motionless, to 30 per square foot per minute when he is exercising fully clothed, or to as many as 150 when dressing and undressing and 200–300 when washing his hands with soap and water. But even when a standard activity is employed, there is great and still unexplained variation in the ability of carriers to disperse their organisms (Hare 1963).

Most of the particles coming from a fully dressed individual while exercising are probably derived from the clothing (Hare & Thomas 1956) but what effects if any are imposed by the type of material (i.e. whether it is woollen, cotton or synthetic fibres) are still unknown. Those from bedding in hospital wards consist of cellulose fibres from the sheets and not, as was at one time thought, protein fibres from the blankets (Rubbo *et al.* 1960, Pressley 1958) but some of the particles may apparently consist of corium from the skin (Davies & Noble 1962).

Although such particles soon sink to the ground and become incorporated in the coarser and heavier masses we know as dust, they are still comparatively small at the time of their liberation. Using the size grading sampler, Williams *et al.* (1956), Lidwell *et al.* (1959), Dumbell *et al.* (1948), Noble (1961), Kingston *et al.* (1962) and Rountree & Beard (1962) have all found that those containing organisms such as *Strep. salivarius* or *Staph. aureus* derived from handkerchiefs, bedding in hospitals or clothing in offices, may be as small as 4 μ or as large as 30 μ, the mean being about 20 μ. This is almost exactly the same size range as that of droplet nuclei containing organisms that are expelled from the human mouth, Lidwell *et al.* (1959) having found that 63·0% of them were between 4 and 18 μ in diameter with 22·9% being smaller and 14·0% larger.

In view of all this, it is to be expected that bacteria-carrying particles from the skin, clothing and bedding will be as capable of remaining suspended in the atmosphere as are those droplet nuclei that carry bacteria. It may well be that they are even more capable of doing so for whereas 10% of such particles liberated from the skin and clothing during exercise remained airborne for 35 minutes, and some for 120 minutes (Duguid & Wallace 1948) only 4% of the droplet nuclei from the human mouth containing organisms remained in suspension for 30 minutes and 2% for 40 minutes in another series of estimations (Bourdillon *et al.* 1942). Furthermore, it has also been shown (Brown & Allison 1937, Rubbo *et al.* 1960, Rubbo *et al.* 1962) that particles containing *Strep. pyogenes*, *Staph. aureus* or a marker organism such as *Staph. citreus*, all derived from sheets or blankets, can similarly remain airborne long enough in hospital wards to become disseminated all over the ward within three hours and may even reach culture plates 9 feet from the floor. Thus, both in dimensions and behaviour, the airborne particles derived from the person and environment resemble closely the bacteria-carrying droplet nuclei produced by a human being when he coughs, sneezes or talks.

The Relative Value of the Different Vehicles by which Pathogenic Organisms may be Transmitted

I mentioned at the start of this Address that swallowing in saliva, expectoration in saliva or sputum, and expulsion in heavy Flugge droplets are all methods by which respiratory organisms can reach the outside world. Some may, as a result, find their way to the respiratory tract of another person. But it is improbable that any of these methods plays an important part in the transmission of respiratory infections in general. This leaves droplet nuclei and particles released from the skin, clothing, bedding and the environment generally for more serious consideration.

Theoretically, the principal attribute of droplet nuclei is that the smallest (which are also the most numerous) can remain airborne for hours and so convey infection over long distances. And it was for this reason that in 1946, Wells, Winslow & Robertson stated categorically that only droplet nuclei are sufficiently mobile to be associated with what these authors describe as 'epidemic phenomena of contagion', the alternative vehicles, that is particles from the skin, clothing and bedding, being considered too heavy and clumsy for this purpose. This doctrine is repeated in the monograph Wells published in 1956.

The evidence produced in support of this is too meagre for serious consideration and that which has accumulated in the meanwhile, to which reference has already been made, shows that the droplet nuclei containing micro-organisms, expelled by a human being when sneezing, coughing or talking, are, in fact, very much larger and that particles from the skin, clothing and bedding that contain organisms, are very much smaller than Wells is evidently prepared to allow. In consequence there is little to choose between the two vehicles in the matter of size and, therefore, mobility.

In ability to convey pathogenic organisms, there are, however, very important differences. There is certainly considerable doubt whether any significant number of the droplet nuclei expelled by a human being are likely to contain organisms belonging to most of the species that can cause infection in the respiratory tract. But on the other hand, particles released from the skin, clothing and bedding have been shown to contain, sometimes in large numbers, pathogenic micro-organisms originating in the nose, tonsils and lungs and there is no reason to suppose that those in the only remaining site in the respiratory tract not yet investigated, the mouth, cannot become airborne in the same way.

It was largely for these reasons that as long ago as 1946 I suggested (Hare & Mackenzie 1946) that this dissemination of contaminated particles from the skin and clothing is what one might call the normal method by which respiratory infections of all kinds are transmitted. Nothing that has emerged since then has rendered this hypothesis untenable. On the contrary, a great deal of confirmatory evidence has in fact been obtained.

REFERENCES

Bloomfield J M
(1921) *Bull. Johns Hopk. Hosp.* 32, 290
(1922*a*) *Amer. Rev. Tuberc.* 5, 903
(1922*b*) *Bull. Johns Hopk. Hosp.* 33, 145
Bloomfield J M & Felty A R
(1924) *Bull. Johns Hopk. Hosp.* 35, 115
Bourdillon R B & Lidwell O M (1941) *Lancet* ii, 365
Bourdillon R B, Lidwell O M & Lovelock J E
(1942) *Brit. med. J.* i 42
Brown W A & Allison V D (1937) *J. Hyg., Camb.* 37, 1
Chapin C V (1910) Sources and Modes of Infection. New York
Chaussé P
(1914*a*) *Ann. Inst. Pasteur* 28, 608
(1914*b*) *Ann. Inst. Pasteur* 28, 721
(1914*c*) *Ann. Inst. Pasteur* 28, 771
(1916) *Ann. Inst. Pasteur* 30, 613
Colebrook L (1933) *Brit. med. J.* ii, 723
Cornet G
(1889) *Z. Hyg. InfektKr.* 5, 191
(1904) Tuberculosis. Ed. W B James. In: Nothnagel's Encyclopedia of Practical Medicine. Philadelphia
Cumming J G (1920) *J. Amer. med. Ass.* 74, 1072
Davies R R & Noble W C (1962) *Lancet* ii, 1295
Doust B C & Lyon A B (1918) *J. Amer. med. Ass.* 71, 1216
Druett H A, Henderson D W, Packman L & Peacock S
(1953) *J. Hyg., Camb.* 51, 359
Duguid J P
(1945) *Edinb. med. J.* 52, 385
(1946*a*) *Brit. med. J.* i, 265
(1946*b*) *J. Hyg., Camb.* 44, 471
Duguid J P & Wallace A T (1948) *Lancet* ii, 845
Dumbell K R, Lovelock J E & Lowbury E J
(1948) *Lancet* ii, 183
Eagleton A J (1919) *J. Hyg., Camb.* 18, 264
Eichenwald J G, Kotsevalov O & Fasso L A
(1959) *Amer. J. Dis. Child.* 98, 432
Flugge C
(1897) *Z. Hyg. InfektKr.* 25, 179
(1899) *Z. Hyg. InfektKr.* 30, 107
Friberger R (1909) *Z. Tuberk.* 13, 37
Gillespie E H, Devenish E A & Cowan S T
(1939) *Lancet* ii, 870
Gloyne S R (1922) *Tubercle* 3, 497
Gordon M H (1916) *Brit. med. J.* i, 849
Green C A, Challinor S W & Duguid J P
(1945) *Ann. Rheum. Dis.* 5, 36
Hamburger M (1944) *J. infect. Dis.* 75, 71
Hamburger M, Green M J & Hamburger V G
(1945) *J. infect. Dis.* 77, 68, 96
Hamburger M, Puck T T, Hamburger V G & Johnson M A
(1944) *J. infect. Dis.* 75, 79
Hare R
(1940) *Canad. publ. Hlth J.* 31, 54
(1941) *Lancet* i, 85
(1963) In: Infection in Hospitals. CIOMS Symposium. Ed. R E O Williams & R A Shooter. Oxford; p 75
Hare R & Cooke E M (1961) *Brit. med. J.* ii, 333
Hare R & Mackenzie D M (1946) *Brit. med. J.* i, 865
Hare R & Ridley M (1958) *Brit. med. J.* i, 69
Hare R & Thomas C G A (1956) *Brit. med. J.* ii, 840
Harper G J (1961) *J. Hyg., Camb.* 59, 479
Harper G J & Morton J D (1953) *J. Hyg., Camb.* 51, 372
Hatch T F & Hemeon W C L (1948) *J. industr. Hyg.* 30, 172
Hemmes H H, Winkler K C & Kool S M
(1960) *Nature, Lond.* 188, 430
Hirshfeld J W & Laube P J (1941) *Surgery* 9, 720
Jennison M W (1941) *Sci. Mon., N.Y.* 52, 24

Kingston D, Lidwell O M & Williams R E O
(1962) *J. Hyg., Camb.* 60, 341
Lange B & Keschischian K K (1925) *Z. Hyg. InfektKr.* 104, 256
Lastschenko (1899) *Z. Hyg. InfektKr.* 30, 125
Lidwell O M, Noble W C & Dolphin G W
(1959) *J. Hyg., Camb.* 57, 299
Noble W C (1961) *J. Path. Bact.* 81, 523
Ostermann A (1908) *Z. Hyg. InfektKr.* 60, 375
Paine C G (1935) *Brit. med. J.* i, 243
Phelps E B & Buchbinder L (1941) *J. Bact.* 42, 321
Pressley T A (1958) *Lancet* ii, 712
Rammelkamp C H, Morris A J, Catanzaro F J, Wannamaker L W,
Chamovitz R & Marple E C (1958) *J. Hyg., Camb.* 56, 280
Riley R L, Mills C C, Nyka W, Weinstock N, Storey P B,
Sultan L U, Riley M C & Wells W F (1959) *Amer. J. Hyg.* 70, 185
Rogers J B (1920) *Amer. J. publ. Hlth.* 10, 345
Rountree P M & Beard M A (1962) *J. Hyg., Camb.* 60, 387
Rubbo S D & Benjamin M (1953) *J. Hyg., Camb.* 51, 278
Rubbo S D, Pressley T A, Stratford B C & Dixson S
(1960) *Lancet* ii, 397
Rubbo S D, Stratford B C & Dixson S
(1962) *Brit. med. J.* ii, 282
Shooter R A, Smith M A & Hunter C J W
(1959) *Brit. J. Surg.* 47, 246
Stillman E G (1917) *J. exp. Med.* 26, 513
Strauss W (1922) *Z. Hyg. InfektKr.* 96, 27
Thomas J C & Van den Ende M (1941) *Brit. med. J.* i, 953
Trillat M A (1938) *Ann. Hyg. publ., Paris* 16, 49
Wells W F
(1934) *Amer. J. Hyg.* 20, 611
(1956) Airborne Contagion and Air Hygiene. Cambridge, Mass.
Wells W F, Ratcliffe H L & Crumb C (1948) *Amer. J. Hyg.* 47, 1
Wells W F & Stone W R (1934) *Amer. J. Hyg.* 20, 619
Wells W F & Wells M W (1936) *J. Amer. med. Ass.* 107, 1698, 1805
Wells W F, Winslow C E A & Robertson E C
(1946) *Amer. J. publ. Hlth* 36, 324
Weyrauch F & Rzymkowski J (1938) *Z. Hyg. InfektKr.* 120, 444
Williams R E O (1946) *J. Path. Bact.* 58, 259
Williams R E O, Lidwell O M & Hirch A
(1956) *J. Hyg., Camb.* 54, 512
Winslow C E A & Robinson E A (1910) *J. infect. Dis.* 7, 17
Wright H D, Shone H R & Tucker J R
(1941) *J. Path. Bact.* 52, 111
Ziesché H (1907) *Z. Hyg. InfektKr.* 57, 50

Meeting November 5 1963

A laboratory meeting was held at the Archway Wing of the Whittington Hospital, London. Demonstrations were given.

Meeting November 19 1963

The subject of the meeting was **Antibiotics for Infections by Gram-negative Bacilli,** and the following papers were read:

The Polymyxins
Dr D A Long (*London*)

The Role of Penicillinases in the Resistance of Gram-negative Bacteria to Penicillins
Dr J T Smith (*London*)

Antibiotics for Proteus Species
Dr Mary Barber and Miss P M Waterworth (*London*)

Meeting February 4 1964

A laboratory meeting was held at the London School of Hygiene and Tropical Medicine.